

Peer Review File

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Reviewer A

The authors have summarized their single-centre experience on tracheal and laryngotracheal resections and reconstructions. As the authors stated, there are very few Nordic reports on this issue. The authors describe their surgical techniques and outcomes after tracheal and laryngotracheal resections due to benign and malignant lesions. Perioperative management, postoperative complications and outcomes are well presented.

The authors conclude that these procedures may be performed safely. Due to their complex nature further centralization is needed and such procedures should be performed primarily at institutes with highly experienced multi-professional teams. I would like to congratulate the authors on this excellent and very well written paper.

REPLY: We thank the Reviewer for the overall positive evaluation and the relevant and constructive comments. Please see our detailed responses below. The changes and additions can be found highlighted in the revised text.

COMMENT: The authors have stated that not all patients underwent preoperative bronchoscopy. In my opinion, the bronchoscopy is a cornerstone of the medical and surgical management of tracheal disease. I would therefore kindly ask the authors to elaborate on this point and thoroughly discuss the conditions, where in their opinion a bronchoscopy is not needed.

REPLY: We agree with the Reviewer regarding the importance of endoscopic examination of each airway lesion. In the present series some of the stenotic lesions caused a severely compromised subglottic airway condition, where a tracheoscopic procedure was considered sufficient for surgical decision making. On urgently treated patients (eg. due to trauma), the bronchoscopy was performed at the time of surgery. Of note, all patients had computed tomography scan performed. We have therefore now clarified this in our text (page 4, lines 2 & 5).

Changes in the text: Page 4, line 2: added to sentence “well in advance”

Page 4, line 5: added to sentence “but at the time of surgery”

Reviewer B

The paper present the results of a small number of patients with different indications for surgery and surgical procedures. The techniques are not innovative and the results are not outstanding. Although this may be a rare report from northern Europe, the didactic or scientific benefit for the thoracic surgeon is not obvious.

REPLY: We thank the Reviewer for this comment.

Reviewer C

Did complications have any relation to length of resection. Did any patient require laryngeal release

to reduce tension? In those patients with recurrent nerve paralysis could lateralization of cord have improved results or avoided tracheostomy. Did past history of tracheostomy influence outcome. Did you have a strategy to deal with post op dyspnea ie heliox, steroids or diuresis. We're ttubes considered as alternative to tracheostomy. What was status of margins for tumors.

REPLY: We thank the Reviewer for these valid questions. We have revised the text of our manuscript accordingly. Please see our detailed responses below. The changes and additions can be found highlighted in the revised text.

COMMENT 1: Did complications have any relation to length of resection.

REPLY 1: Statistical analysis did not show any significant correlation between the length of resection and postoperative complications. Please, also see our response 15 for Reviewer D.

COMMENT 2: Did any patient require laryngeal release to reduce tension.

REPLY 2: A proper laryngeal release procedure was only performed in one patient with a 5-cm-long resection, and we have now commented this in the Results part (page 5, line 21).

Changes in the text: Page 5, line 21: **"One patient required a laryngeal release to reduce tension due to a 5-cm-long resection"**

COMMENT 3: In those patients with recurrent nerve paralysis could lateralization of cord have improved results or avoided tracheostomy.

REPLY 3: For patients who needed a tracheostomy, the ENT team always considered the possibility of doing a lateralization of cord before performing a permanent tracheostomy. We have now addressed this in our text (page 7, lines 28-30).

Changes in the text: Page 7, lines 28-30: **"For patients who needed a tracheostomy, the Otorhinolaryngology – Head and Neck Surgery team always considered the possibility of a vocal cord lateralization before performing a permanent tracheostomy."**

COMMENT 4: Did past history of tracheostomy influence outcome.

REPLY 4: A previous tracheostomy may indeed be a risk factor for postoperative complications. However, we could not find a clinically significant correlation between these as only four out of the 13 patients with a previous tracheostomy experienced a postoperative complication. We have now discussed this issue in our revised paper (page 7, lines 19).

Changes in the text: page 7, line 19: **"As only 4 out of the 13 patients with a previous tracheostomy experienced a postoperative complication, we could not find a clinically significant correlation between these factors."**

COMMENT 5: Did you have a strategy to deal with post op dyspnea ie heliox, steroids or diuresis. We're ttubes considered as alternative to tracheostomy.

REPLY 5: Our postoperative treatment protocol includes the use of steroids, diuretics and racemic adrenalin but not the use of heliox therapy. We do not use T-tubes in the routine treatment of these patients. However, T-tubes may offer an option to avoid tracheostomies. We

have now this discussed this in the text (page 7, line 11).

Changes in the text: Page 7, line 11: “Our postoperative treatment protocol includes the use of steroids, diuretics and racemic adrenalin but not the use of heliox therapy. We do not use T-tubes in the routine treatment of these patients. However, T-tubes may offer an option to avoid tracheostomies.”

COMMENT 6: What was status of margins for tumors.

REPLY 6: We achieved R0 resection on all but one patient with malignant tumor, we have included this statement in the Results part (page 6, lines 8 & 11).

Changes in the text: Page 6, line 8: “R0 resection was achieved in all but one of these patients.”
Page 6, line 11: “(residual tumor in margin)”

Reviewer D

The authors describe their single-institution experience on tracheal and cricotracheal resection in 44 patients. We congratulate the authors on their work. Please find the comments below.

REPLY: We thank the Reviewer for the thorough evaluation and the comprehensive comments. Please see our detailed responses below. The changes and additions can be found highlighted in the revised text.

Introduction

COMMENT 1: Please refrain from the use of abbreviations such as ATS and ALTS as these are not common and trouble reading.

REPLY 1: This has been corrected accordingly (page 3, lines 5 & 12-13)

Changes in the text: Page 3, lines 5 & 12-13: “ATS” and “ALTS” corrected to “Acquired benign tracheal stenosis” and “Acquired benign laryngotracheal stenosis

COMMENT 2: It is not entirely clear what this study adds to the existing ones? Apart that there are only few, what are their limitations that are being overcome by the current one.

REPLY 2: We thank the Reviewer for this consideration. The present study aims at demonstrating the currently available surgical approach for the management of either neoplastic or benign stenosis causing laryngotracheal lesions. Our emphasis is to present both the nature of various lesions and the long-term outcome including complications. These data are continuously needed in the evaluation and management decision making in the care of this patient population. The patient series is heterogeneous in terms of etiology of the lesions, but the main aim is to provide the readers information on the available surgical approach as this still is, and should be performed, on a limited number of centres.

COMMENT 3: In addition, it would be better to form a more strict research question. For example, complications after tracheal resection. Doing this, the results section can be divided in more and less important results. Now the results section seems a summation of all results without weighing.

REPLY 3: We state in the end of introduction that our focus was on surgical complications. In order to make this clearer, we omitted descriptive details on page 5 in order to make the Results section shorter and point out the importance of the complication chapter.

Changes in the text: Page 5, line 3: Removed 1st paragraph

Page 5, line 28: Added heading “**Complications**”

Methods

COMMENT 4: When reporting the median value, please also provide the interquartile range instead of the range.

REPLY 4: This has been corrected accordingly and we now present IQR when median value is presented (Pages 1, 5, 11 & 13).

Changes in the text: Page 1, lines 16-17; page 5, lines 19, 21, 23-24; page 11, table 1; page 13, table 3: “**Range**” corrected to “**IQR**”

COMMENT 5: Was the study approved by an ethics committee? In addition, was informed consent obtained?

REPLY 5: This has now been included in the text accordingly (page 3, line 31; page 9, line 5).

Changes in the text: Page 3, line 31: “**This study is a retrospective hospital chart review and therefore, no research ethics approval was needed. An institutional research permission was granted**”

Page 9, line 5: “As this study only involved review of patient charts and none of the patients were contacted, no consent form or ethics committee approval was needed.” corrected with “**This study is a retrospective hospital chart review and therefore, no research ethics approval was needed. An institutional research permission was granted**”

COMMENT 6: What was the reason to perform flexible bronchoscopy in only part of patients?

REPLY 6: Please, see the response for the Reviewer A.

COMMENT 7: What was the rationale to routinely use muscle flaps?

REPLY 7: We admit that the use of muscle flaps is controversial. We have felt that in our hands it has worked well in order to avoid any air leak from the anastomosis, but we admit that it may be a bit excessive. We have now added a statement regarding this in the text.

Changes in the text: Page 4, line 27: added to sentence “**from the adjacent tissues to enhance the volume of vital tissue and blood supply in that area and to decrease the risk of air leakage**”

COMMENT 8: What is the maximum length of the stenotic segment which can be resected with primary anastomosis without the need for an interponent? I.e., what patients were not fit for resection?

REPLY 8: We feel that maximum length of resection is about 5 cm or half of the tracheal length. We have now added a sentence in the Discussion part of our paper to point this out (page 7, line 2).

Changes in the text: Page 7, line 2: **“We consider the maximum length of a safe resection to be about 5 cm, or half of the tracheal length.”**

COMMENT 9: Please incorporate the STROBE guidelines.

REPLY 9: The STROBE document has been submitted accordingly.

COMMENT 10: Please define the complications. For example, when was a bleeding considered as complication? Based on amount, or based on the need for additional interventions?

REPLY 10: In the classification of our complications, we used the Clavien-Dindo classification, where the need of intervention makes the complication more severe.

Results

COMMENT 11: If talking about significant morbidities, the term “significant morbidities” should first be clearly defined in the methods section.

REPLY 11: We admit that the term significant comorbidities was inadequate. Please, also see response 3. We have omitted descriptive details on page 5 and consequently this statement. We have done so in order to make the Results section shorter and point out the importance of the complication chapter.

Changes in the text: Page 5, line 3: Removed 1st paragraph.

COMMENT 12: 16% of patients still required permanent tracheostomy postoperatively. If these patients were not operated due to a tumor, was it retrospectively even indicated to perform resection? Given that the primary goal is to reestablish a functioning airway and the fact that this complication rate is considerably higher compared to other series.

REPLY 12: Two out of the seven patients that required a permanent tracheostomy were operated due to a benign lesion. These two patients were challenging, as one of them suffered from an idiopathic stenosis and one from an IgG4-related disease (reported in the original text, Results part, last paragraph), both of which resulted in resistant stenoses despite various bronchoscopic interventions. The surgical resection was conducted as a final attempt to avoid a permanent tracheostomy. We have now addressed this in the text accordingly.

Changes in the text: Page 6, line 16: added **“Although the decision to perform a resection was primarily aimed at securing a patent airway, one of the idiopathic stenosis patients and the patient with IgG4-related disease ultimately required a permanent tracheostomy.”**

COMMENT 13: In 4 patients, dysphonia was present which can be due to laryngeal recurrent nerve palsy. Wouldn't it retrospectively have been better to identify the nerves during surgery in order to prevent their damage?

REPLY 13: Four patients with dysphonia give a reason to consider the improvement of

recognition of laryngeal nerves during surgery in order to avoid damaging the nerves in the future. We have now discussed this accordingly in our text (please see response 16).

COMMENT 14: Please also see the last comment under introduction.

REPLY 14: Please, see our response for comment 3.

COMMENT 15: A statistical analysis part is missing.

REPLY 15: Although statistical analyses were performed, they did not show any significant results due to the low volume and heterogenic cohort of patients. Therefore, these analyses were deemed insignificant and were not included in the study. This statement has been added in the Results part of the text (page 5, line 25), as well as a description of how the analyses were performed in the Methods (page 4, line 10).

Changes in the text: Page 4, line 10: Added heading “Statistical analysis”

Page 4, line 11: “Continuous data are expressed as median and interquartile range (IQR), as none of the variables were normally distributed. Categorical data are summarized as proportions and percentages. Differences between two groups in continuous variables were compared with the Mann-Whitney U test and in categorical variables with the Chi-squared test. Statistical analyses of patient and stenosis characteristics as well as treatment factors were performed to identify potential factors predicting treatment failure or high incidence of complications. Data were analyzed using IBM SPSS Statistics (version 25, IBM Corporation)”

Page 5, line 25: “Although statistical analyses were performed, they did not show any reliable results due to the low volume and heterogenic cohort of patients. Therefore, these analyses were deemed insignificant and were not included in the study.”

Discussion

COMMENT 16: What can we learn from this study regarding the prevention of complications occurred?

REPLY 16: Our study clearly showed the spectrum of typical complications after tracheal- and cricotracheal resections. We can learn from this study that thorough preoperative investigations and careful planning, as well as all the preventive measures at the time of surgery, including the recognition of laryngeal nerves, are needed in order to avoid these complications. We have now discussed this in our text (page 8, line 18)

Changes in the text: Page 8, line 18: “Our study clearly showed the spectrum of typical complications after these procedures. We can learn from this study that thorough preoperative investigations and careful planning, as well as preventive measures at the time of surgery are needed in order to avoid these complications.”

COMMENT 17: 44 cases in 15 years is less than 3 a year. Were all cases performed by a single surgeon?

REPLY 17: The operations were performed by one of three thoracic surgeons in collaboration with an otorhinolaryngologist – head and neck surgeon. This has been added to the Results (page 5, line 3)

Changes in the text: Page 5, line 3: **“The operations were performed by one of three thoracic surgeons in collaboration with an otorhinolaryngologist – head and neck surgeon.”**

COMMENT 18: The success rate of 75% is a new result being introduced in the discussion section; please incorporate in the results section. In addition, please define “success” in the methods section as it is a multi-interpretable term. Because success can be also be defined from the patient’s perspective, a patent airway etc.

REPLY 18: We agree with the Reviewer and have now added this information in the Results part (page 5, line 37). The definition for the term success has been added to the Methods part (page 4, line 8).

Changes in the text: Page 4, line 8: **“Postoperative success was defined as the patient not requiring reoperation or postoperative interventions.”**

Page 5, line 37: **“Overall success rate was 75% (no need for reoperations or postoperative interventions)”**

COMMENT 19: You found that patients after CTR suffered from more complications than after TR, however, this is not consolidated by statistical analysis. In addition, this is a rather bold statement given the heterogeneity and low sample size in both groups.

REPLY 19: We admit that this statement is too bold, and we have now corrected it in the text accordingly (page 7, line 37).

Changes in the text: Page 7, line 37: “In our study, we found that patients after CTR suffered from more complications than patients after TR, which is in line with previous studies.” rephrased to **“In line with previous studies, our patients who underwent CTR also suffered from several complications.”**

Page 7, paragraph 1: Removed **“We also found that patients undergoing CTR suffered from more complications than patients after TR.”**

COMMENT 20: Combining both malignant and benign cases just for the sake of sample size seems ambiguous since it incorporates such an amount of heterogeneity that comparison becomes even more difficult.

REPLY 20: The present study aims at demonstrating the currently available surgical approach for the management of either neoplastic or benign stenosis causing laryngotracheal lesions. Our emphasis is to present both the nature of various lesions and the long-term outcome including complications. These data are continuously needed in the evaluation and management decision making in the care of this patient population. The patient series is heterogenous in terms of etiology of the lesions and we admit that it makes the comparison challenging, but we feel that this gives an opportunity to form an overall understanding of the different complications which are related to these resections. The main aim is to provide the readers information on the available surgical approach as this still is, and should be performed, on a limited number of centres.

COMMENT 21: Conclusion: (crico)tracheal resection is considered safe, however, the authors state

a complication rate of 46%? In addition, 'high' success rate is subjective given that ¼ patients have a non-successful treatment.

REPLY 21: Our conclusion is that the resections were considered safe as our 30-day mortality was zero and only 5 patients in the benign group had Clavien-Dindo grade IIIA or higher complications. We admit that the success rate was not excellent because 25 % of patients had a non-successful outcome. Therefore, we have rephrased “high success rates” to “acceptable outcomes” in the Discussion part (page 8, line 16)

Changes in the text: Page 8, line 16: “high success rates” rephrased to “acceptable outcomes”